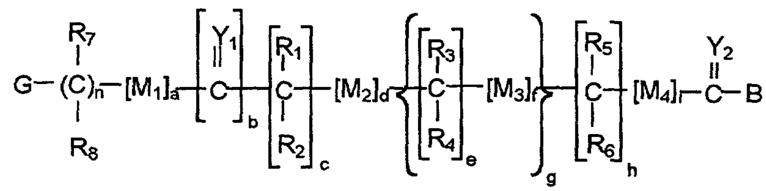
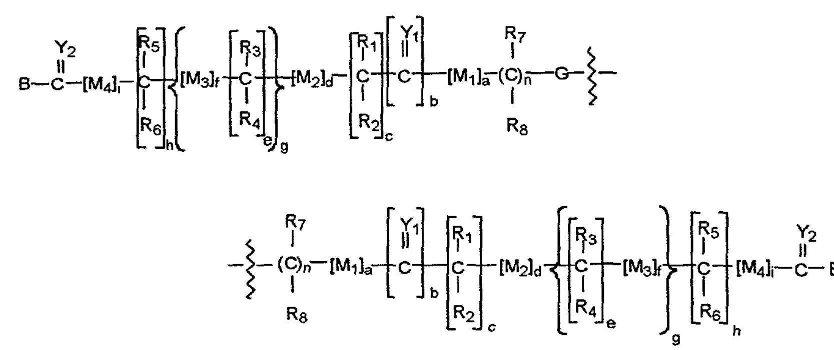
ABSTRACT

The present invention is directed to methods of preparing polymeric conjugates of biologically active agents of the formula:



(I)

wherein G is a linear or branched polymer residue; Y_1 and Y_2 are independently O, S, or NR_9; M_1-M_3 are independently O, S, or NR_{10}; M_4 is X or Q; wherein X is an electron withdrawing group and Q is a moiety containing a free electron pair positioned three to six atoms from $C(=Y_2)$; B is a residue of an amine-containing moiety or a residue of a hydroxyl-containing moiety; R_{1-10} are independently selected from the group consisting of hydrogen, C_{1-6} alkyls, C_{3-12} branched alkyls, C_{3-8} cycloalkyls, C_{1-6} substituted alkyls, C_{3-8} substituted cycloalkyls, aryls, substituted aryls, aralkyls, C_{1-6} heteroalkyls and substituted C_{1-6} heteroalkyls; *a, b, c, d, e, f, g, h, i* and *n* are each independently zero or a positive integer. In preferred aspects, the polymer transport system di-substituted with an equivalent of the active ingredient on both the proximal and distal ends of the polymer, as shown in the formula below:



(II)

Methods of preparing the same and methods of treatment using the same are also included as part of the present invention.